

Support for the amendments

The amendments to the claims are fully supported in the claims as filed, and thus do not represent new matter.

Remarks

1. Claim rejections under 35 USC 112, second paragraph

(a) Claim 21 was rejected as indefinite based on the assertion that it is not clear how the method is correlated to neurite outgrowth. The Applicants traverse this rejection, as the claim clearly details a method for identifying neurites extending from cell bodies (21(d)) and determining one or more neurite features, which one of skill in the art would clearly understand as correlating to neurite outgrowth (Claim 21(e)). However, in order to expedite prosecution, the Applicants have amended the claim to include a clause stating that the features provide a measure of neurite outgrowth from the cell bodies. The Applicants note that this added clause does not narrow the scope of the claim. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(b) Claim 21 was rejected as indefinite based on the assertion that it is not clear how the nuclear image and the neurite image will be employed to measure neurite outgrowth. The patent office asserted that “the claims merely require two separate imagings of the nucleus and neurite, but does not identify how the images will be related to each other or will measure neurite outgrowth.” The Applicants traverse this rejection.

Claim 21(b) recites obtaining a nuclear image and a neurite image. 21(c) recites that cell bodies are identified from the nuclear image. 21(d) recites identifying neurites (identified in the neurite image) extending from cell bodies (which were identified in the nuclear image as recited in 21(c))). 21(e) then recites specific features of the neurons that are determined and which provide a measure of neurite outgrowth. Thus, the patent office’s assertion that the claim does not identify how the images will be related to each other or how they will be used to measure neurite outgrowth is incorrect. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(c) Claim 21 was rejected as indefinite based on the assertion that the term “possess” is indefinite. The Applicants traverse this rejection. The phrase “the cells possess one or more luminescently labeled reporter molecules” is clearly defined on page 69 lines 4-10, as including the situations where the luminescent reporter molecule is expressed as a luminescent reporter molecule by the cells, wherein it is added to the cells as a luminescent reporter molecule, or is

luminescently labeled by contacting the cell with a luminescently labeled molecule that binds to the reporter molecule. Thus, one of skill in the art is clearly apprised of the meaning of the term “possess” in the context of claim 21. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(d) Claim 21 was rejected as indefinite based on the assertion that the limitation in step 21(d) “the cell bodies from the neurite image” lacks antecedent basis in step 21(b). The Applicants traverse this rejection. Step 21(c) recites “automatically identifying cell bodies from the nuclear image.” Step 21 (d) recites “identifying neurites extending from the cell bodies from the neurite image.” As discussed above, this step recites that neurites are automatically identified from the neurite image and correlated as extending from the cell bodies identified in 21(c). Thus, the term “the cell bodies” in step 21(d) derives antecedent basis from “cell bodies” as recited in 21(c). Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(e) Claim 22 was rejected as indefinite based on the assertion that those of skill in the art would not understand whether the term “cell bodies” means the cell bodies in claim 21 step (c) or step (d). The Applicants traverse this rejection.

As discussed above, Step 21(c) recites “automatically identifying cell bodies from the nuclear image.” Step 21 (d) recites “identifying neurites extending from the cell bodies from the neurite image.” As discussed above, this step recites that neurites are automatically identified from the neurite image and correlated as extending from the cell bodies identified in 21(c). Thus, the term “the cell bodies” in step 21(d) derives antecedent basis from “cell bodies” as recited in 21(c). Therefore, the term “cell bodies” in steps (c) and (d) of claim 21 are the same cell bodies, and thus the term “cell bodies” in claim 22 are the cell bodies of both steps (c) and (d) in claim 21. Thus, those of skill in the art would not find claim 22 indefinite, and the Applicants respectfully request reconsideration and withdrawal of this rejection.

(f) Claims 22 and 24 were rejected as indefinite based on the assertion that the terms “kernel”, “conditional”, and “set of nodes” are relative terms which render the claim indefinite. The Applicants traverse this rejection.

“Kernel Image”: Claim 22 recites “generating a kernel image from the nuclear image.” The specification defines how a kernel image is generated. On page 79, line 19-20 the specification states that a binary image is generated for the nuclear channel image by auto-thresholding, and that “one coordinated component is present in this kernel image ...” Thus, the specification makes clear to those of skill in the art that a “kernel image” derived from a nuclear image is a binary image of the nuclear image generated by auto-thresholding.

“Conditional dilations”: This term is defined on page 80, lines 7-10:

“The dilations performed are termed *conditional dilations*; each time the dilation is applied, a layer of one pixel is added to the kernel on the condition that the pixels in that layer are present in the neuron reservoir image.”

Thus, those of skill in the art would clearly understand the meaning of “conditional dilations.

“Set of Nodes”: The term “node” is clearly defined in the specification on page 81 lines 8-9: “Each connected component in the dilation image is termed a *node*.” Those of skill in the art would thus understand that “determining a set of nodes from the dilation image” simply means determining a group of connected components from the dilation image.

Thus, the Applicants respectfully request reconsideration and withdrawal of these rejections.

(g) Claims 25 and 29 were rejected as indefinite based on the assertion that it was unclear what was meant by the steps being conducted “at multiple time points.” The Applicants have amended claims 25 and 29 to clarify that the recited series of steps are carried out at more than one time point. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(h) Claims 26 and 27 were rejected as indefinite based on the assertion that the term “neurons” lacked antecedent basis. The Applicants have amended the claims to obviate the rejection, and thus respectfully request reconsideration and withdrawal of the rejection.

(i) Claim 28 was rejected as indefinite based on the assertion that those of skill in the art would not understand whether the term “cell bodies” means the cell bodies in claim 21 step (c) or step (d). The Applicants traverse this rejection.

As discussed above, Step 21(c) recites “automatically identifying cell bodies from the nuclear image.” Step 21 (d) recites “identifying neurites extending from the cell bodies from the neurite image.” As discussed above, this step recites that neurites are automatically identified from the neurite image and correlated as extending from the cell bodies identified in 21(c). Thus, the term “the cell bodies” in step 21(d) derives antecedent basis from “cell bodies” as recited in 21(c). Therefore, the term “cell bodies” in steps (c) and (d) of claim 21 are the same cell bodies, and thus the term “cell bodies” in claim 28 are the cell bodies of both steps (c) and

(d) in claim 21. Thus, those of skill in the art would not find claim 28 indefinite, and the Applicants respectfully request reconsideration and withdrawal of this rejection.

2. Claim rejections under 35 USC 103(a)

(a) Claims 21, 26-27, 29, and 30-32 were rejected as being obvious over the combination of Dow (Cytometry 25:7-81 (1996) in view of McFarlane (Clin. and Eptl. Pharmacol. and Physiol. 1995, 22:363-363) as supported by Wang et al. (Pure and Applied Chemistry 2001, 73(10)1599-1611).

In order to establish a *prima facie* case of obviousness the patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of one of skill in the art to combine or modify the references; 2) a reasonable expectation of success; and 3) the prior art references alone or in combination must teach or suggest *all* the claim limitations. MPEP § 706.02(j).

As an initial matter, the Applicants note that the Wang reference was published in 2001. The present application was filed on November 20, 2000. Thus, the Wang reference is not available as prior art against the current application.

The combination of the cited references does not teach at least the following limitations of the method of presently pending 21:

-providing an array of locations comprising cells,...wherein the cells possess at least a second luminescently labeled reporter molecule that reports on neurite outgrowth;

-obtaining a neurite image from the at least second luminescently-labeled reporter molecule;

-automatically identifying neurites extending from the cell bodies from the neurite image; and

-automatically determining one or more neurite features selected from the group consisting of:

- [i] ~~Total neurite length from all cells;~~
- ii) Total number of neurite branches from all cells;
- iii) Number of neurites per cell;
- iv) Number of neurites per positive neuron;
- v) Neurite length from each cell;
- vi) Neurite length per positive neuron;
- vii) Neurite length per neurite;
- viii) Number of cells that are positive for neurite outgrowth;
- ix) Percentage of cells positive for neurite outgrowth;
- x) Number of branches per neuron; and
- xi) Number of branches per neurite;

wherein the features provide a measure of neurite outgrowth from the cell bodies.

Dow simply teaches typing T-cells in tissue sections using nuclear stains and T-cell specific antigens. Dow says nothing about neurites or their measurement in any way. The “splines” mentioned in Dow are not part of the cells, but are instead an image processing technique for boundary determinations (see page 76 left column, lines 6-11 of the paragraph with heading “Cell boundary determination”). McFarlane teaches measuring a total amount of neurite outgrowth for an entire area of cells, and provides no teaching or suggestion as to how to determine any other neurite feature, much less the specific neurite features recited in claim 21, which are determined by the methods of the present invention. Thus, the combination of Dow and MacFarlane fail to teach or suggest at least the limitations from claim 21 described above. Thus, the combination of Dow and MacFarlane does not make the invention of claim 21 obvious to those of skill in the art, under MPEP § 706.02(j).

Claims 26-27, 29, and 30-32 are dependent upon claim 21, and thus these claims are also not obvious over the cited references to those of skill in the art.

Therefore, the Applicants respectfully request reconsideration and withdrawal of the rejection.

(b) Claim 22 was rejected as being obvious over the combination of Dow (Cytometry 25:7-81 (1996) in view of McFarlane (Clin. and Eptl. Pharmacol. and Physiol. 1995, 22:363-363) as supported by Wang et al. (Pure and Applied Chemistry 2001, 73(10)1599-1611) and further in view of Ranefall (Analyt. Cellul. Pathol. 15:145-156 (1997)). The Applicants traverse this rejection.

In order to establish a *prima facie* case of obviousness the patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of one of skill in the art to combine or modify the references; 2) a reasonable expectation of success; and 3) the prior art references alone or in combination must teach or suggest *all* the claim limitations. MPEP § 706.02(j).

Claim 22 is dependent upon claim 21, and thus includes all of the limitations of claim 21. The combination of the cited references does not teach at least the following limitations of the method of presently pending 22:

-providing an array of locations comprising cells,...wherein the cells possess at least a second luminescently labeled reporter molecule that reports on neurite outgrowth;

-obtaining a neurite image from the at least second luminescently-labeled reporter molecule;

-automatically identifying neurites extending from the cell bodies from the neurite image; and

-automatically determining one or more neurite features selected from the group consisting of:

- [i] ~~Total neurite length from all cells;~~
- ii) Total number of neurite branches from all cells;
- iii) Number of neurites per cell;
- iv) Number of neurites per positive neuron;
- v) Neurite length from each cell;
- vi) Neurite length per positive neuron;
- vii) Neurite length per neurite;
- viii) Number of cells that are positive for neurite outgrowth;
- ix) Percentage of cells positive for neurite outgrowth;
- x) Number of branches per neuron; and
- xi) Number of branches per neurite;

wherein the features provide a measure of neurite outgrowth from the cell bodies.

The Dow, McFarlane, and Wang references are discussed above. The addition of Ranefall does not cure the deficiency of the recited combination of references. The combination of these four references does not teach or suggest at least the above-cited limitations of pending claim 22. It should be further noted that the Ranefall reference also does not teach or suggest the specific limitations of claim 22, which the patent office has acknowledged are not taught or suggested by the combination of Dow and McFarlane. Thus, the combination of the cited references does not make the invention of claim 22 obvious to those of skill in the art, under MPEP § 706.02(j). Therefore, the Applicants respectfully request reconsideration and withdrawal of the rejection.

(c) Claim 28 was rejected as being obvious over the combination of Dow (Cytometry 25:7-81 (1996) in view of McFarlane (Clin. and Eptl. Pharmacol. and Physiol. 1995, 22:363-363) as supported by Wang et al. (Pure and Applied Chemistry 2001, 73(10)1599-1611) and further in view of Sano (Current Trends in Neurochemistry 1997, 1:27-40 (Abstract only)). The Applicants traverse this rejection.

In order to establish a *prima facie* case of obviousness the patent office must establish three criteria; 1) a suggestion or motivation found within the prior art or within the knowledge of

one of skill in the art to combine or modify the references; 2) a reasonable expectation of success; and 3) the prior art references alone or in combination must teach or suggest *all* the claim limitations. MPEP § 706.02(j).

Claim 28 is ultimately dependent upon claim 21, and thus includes all of the limitations of claim 21. The combination of the cited references does not teach at least the following limitations of the method of presently pending 22:

-providing an array of locations comprising cells,...wherein the cells possess at least a second luminescently labeled reporter molecule that reports on neurite outgrowth;

-obtaining a neurite image from the at least second luminescently-labeled reporter molecule;

-automatically identifying neurites extending from the cell bodies from the neurite image; and

-automatically determining one or more neurite features selected from the group consisting of:

- [i] ~~Total neurite length from all cells;~~
- ii) Total number of neurite branches from all cells;
- iii) Number of neurites per cell;
- iv) Number of neurites per positive neuron;
- v) Neurite length from each cell;
- vi) Neurite length per positive neuron;
- vii) Neurite length per neurite;
- viii) Number of cells that are positive for neurite outgrowth;
- ix) Percentage of cells positive for neurite outgrowth;
- x) Number of branches per neuron; and
- xi) Number of branches per neurite;

wherein the features provide a measure of neurite outgrowth from the cell bodies.

The Dow, McFarlane, and Wang references are discussed above. The addition of Sano does not cure the deficiency of the recited combination of references. The combination of these four references does not teach or suggest at least the above-cited limitations of pending claim 28. Thus, the combination of the cited references does not make the invention of claim 28 obvious to those of skill in the art, under MPEP § 706.02(j). Therefore, the Applicants respectfully request reconsideration and withdrawal of the rejection.

Based on all of the above, the Applicants believe the claims are now allowable. If there are any questions or comments regarding this response, the Examiner is encouraged to contact the undersigned agent as indicated below.

Respectfully submitted,

Date: 6/23/04



David S. Harper
Registration No. 42,636

Telephone: 312-913-0001
Facsimile: 312-913-0002

McDonnell Boehnen
Hulbert & Berghoff, Ltd.
300 South Wacker Drive
Chicago, IL 60606